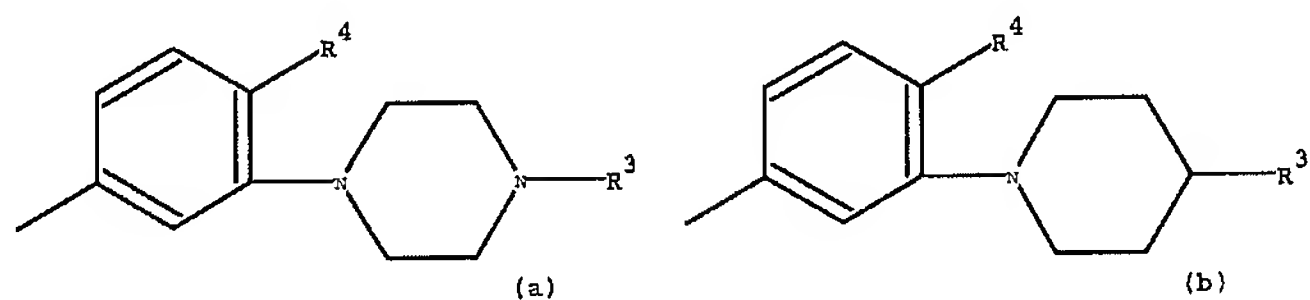


1999-358820/31 B05 MERE 1997.12.17
 MERCK PATENT GMBH *DE 19756036-A1
 1997.12.17 1997-1056036(+1997DE-1056036) (1999.06.24) C07D
 401/04, A61K 31/405, 31/445, C07D 403/04, 491/10, 401/14, 209/18
**New indole amide derivatives - useful as serotonin antagonists
 and reuptake inhibitors, especially antidepressants and
 anxiolytics**
C1999-106360
 Addnl. Data: MATZEN L, VAN AMSTERDAM C, GREINER H,
 RAUTENBERG W, BOETTCHER H, BARTOSZYK G,
 HARTING J

B(6-D1, 14-C3, 14-E10, 14-F2B, 14-J1, 14-L6) .6

1,4-piperidinylene, optionally partially dehydrogenated;



Indole derivatives of formula $R^1-(CH_2)_n-(Y)_q-(Z)_r-CO-NH-R^2$ (I)
 and their salts are new.

R^1 = 3-indolyl optionally mono- or disubstituted by A, OA, OH,
 Hal, CN, NO₂, NH₂, NHA, NA₂, COA, CONH₂, CONHA, CONA₂,
 CH₂OH, CH₂OA, CH₂NH₂, CH₂NHA, CH₂NA₂, COOH and/or
 COOA;

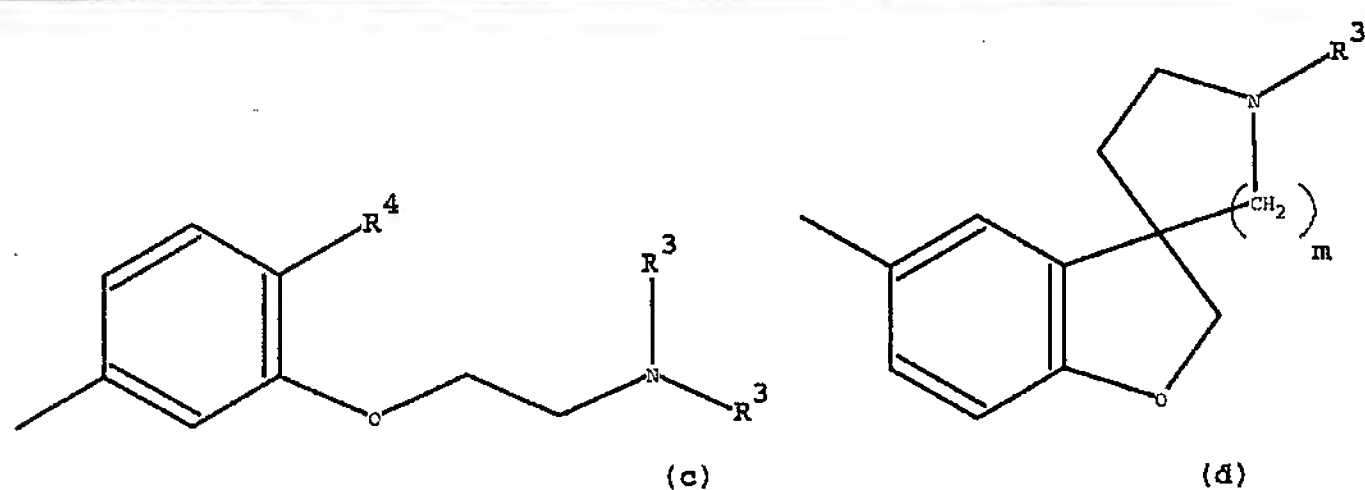
R^2 = a group of formula (a)-(d):

$m = 1$ or 2 ;

$n = 0-4$;

$Y = 1,4$ -cyclohexylene, 1,3-pyrrolidinylene, 1,4-piperazinylene or

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$Z = (CH_2)_n$ or $(CH_2)_nNH$;

$q = 0$ or 1 ;

$r = 0$ or 1 ;

$R^3 = A$;

$R^4 = OA$;

Hal = F, Cl, Br or I;

A = 1-6C alkyl;

provided that r and q are not both 0.

USE

(I) are 5-HT_{1B/D} antagonists and 5-HT (serotonin) reuptake
 inhibitors especially useful as antidepressants and anxiolytic

agents. They can also be used to treat other CNS disorders,
 inflammation, stroke, side effects of neuroleptics, Parkinson's
 disease, Alzheimer's disease symptoms, amyotrophic lateral
 sclerosis, brain and bone-marrow trauma, hypertension, endocrine
 disorders and gastrointestinal disorders, and as pharmaceutical
 intermediates.

PREPARATION

Claimed processes include:

- reacting R^2NH_2 with $R^1-(CH_2)_n-(Y)_q-(Z)_r-CO-L$. $L = Cl, Br, I$ or
 OH ; and
- reacting R^2NH_2 with $R^1-(CH_2)_n-(Y)_q-(Z)_r-H$ in the presence of a
 coupling agent such as 1,1'-carbonyldiimidazole, diphosgene,
 triphosgene or a chloroformate ester.

EXAMPLE

A mixture of 4-methoxy-3-(4-methyl-1-
 piperazinyl)aniline.2HCl (2.65 g), triethylamine (4.5 ml) and 1,1'-
 carbonyldiimidazole (1.6 g) in 125 ml MeCN was stirred at room
 temperature for 3 hr, treated with a suspension of 2 g 5-fluoro-3-(4-
 piperidinyl)-1H-indole and 1.3 ml triethylamine in 125 ml MeCN,

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stirred at room temperature for 12 hr, and worked up. The residue
 was dissolved in acetone, precipitated with 1N HCl and
 recrystallised from ethanol/ether to give 4-(5-fluoro-1H-indol-3-yl)-
 N-(4-methoxy-3-(4-methyl-1-piperazinyl)phenyl)-piperidine-1-
 carboxamide.HCl, m.pt. 231°C. (CD)
 (11pp367DwgNo.0/0)

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